cell, and, in the case of bispecific antibodies, bind by their Fc portion to Fc receptor-positive cells, or in the case of trispecific antibodies, bind by a third specificity to Fc receptor-positive cells---.

On page 27, line 6, after "Fig." insert ---1, parts A and B---.

IN THE CLAIMS:

Cancel claims 24, 25, 28, 29, and 30, and amend claims 1, 13, 14, 17, 18, 23, and 27 as follows. Please note that the brackets in these claims are part of the claim recitations. These claims are shown in marked-up form at the end of this document to clearly show the changes that are being made by this amendment.

1. (three times amended) Method for the preparation of an antibody-tumor cell preparation for immunization of humans and animals against tumor cells comprising the steps of:

a) isolating autologous tumor cells;

b) treating the tumor cells to prevent the survival thereof following reinfusion;

c) incubating the thus treated tumor cells with intact heterologous bispecific antibodies showing the following properties:

(i) binding to a T cell;

(ii) binding to at least one antigen on a tumor cell;

(iii) binding, by their Fc portion to Fc receptor-positive cells; and

(iv) capable of activating the Fc receptor-positive cell whereby the expression of cytokines, co-stimulatory antigens or both is induced or increased,

wherein the bispecific antibodies have isotype combinations selected from the group consisting of:

rat-IgG2b/human-IgG1,

rat-IgG2b/human-IgG2,

rat-IgG2b/human-IgG3[oriental allotype G3m(st) = binding to protein A],

rat-IgG2b/human-IgG4,

rat-IgG2b/rat-IgG2c,

mouse-IgG2a/human-IgG3[caucasian allotypes G3m(b+g) = no binding to protein A, in the following indicated as *],

mouse-IgG2a/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-IgG2a/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human- IgG3*-[CH2-CH3],

mouse-IgG2a/human-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-[VH-CH1,VL-CL]-human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-[VH-CH1,VL-CL]-human-IgG4/rat-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2: > aa position 251]-human-IgG3*[CH3],

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge-CH2-CH3],

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG2-[hinge-CH2-CH3],

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG3-[hinge-CH2-CH3, oriental allotype],

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG4-[hinge-CH2-CH3],

human-IgG1/human-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position 251]-human-IgG3*[CH3],

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position 251]-human-IgG3*[CH3],

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG2[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position 251]-human-IgG3*[CH3],

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG2[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position 251]-human-IgG3*[CH3],

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

human-IgG2/human-[VH-CH1,VL-CL]-human-IgG2-[hinge]-human-IgG3*-[CH2-CH3],

human-IgG4/human-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG3*-[CH2-CH3],

human-IgG4/human-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3*[C-terminal region of CH2 : > aa position 251]-human-IgG3*[CH3],

mouse-IgG2b/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-IgG2b/human-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3*-[CH2-CH3],

mouse-[VH-CH1,VL-CL]-human-IgG4/rat-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4-[CH2]-human-IgG3*-[CH3],

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4-[CH2]-human-IgG3*-[CH3],

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4-[CH2]-human-IgG3*-[CH3],

human-IgG4/human-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4-[CH2]-human-IgG3*-[CH3], and

rat/mouse.

13. (twice amended) A method for preparing a vaccine comprising an antibody-tumor cell preparation, said method comprising preparing an antibody-tumor cell preparation by the method of claim 1, and preparing a vaccine from said antibody-tumor cell preparation.

14. (twice amended) A method for preparing a vaccine comprising activated peripheral blood mononucleated cells, said method comprising preparing an antibody-tumor cell preparation by the method of claim 1 in which step (c) comprises incubating the thus-treated tumor cells with both said intact heterologous bispecific antibodies and peripheral blood mononucleated cells, thereby activating said peripheral blood

mononucleated cells, and (d) preparing a vaccine from the thus-activated peripheral blood mononucleated cells.

17. (twice amended) Method according to claim 14 in which said incubation of step (c) is performed for a period of 1 to 14 days.

18. (twice amended) Method according to claim 14 in which said incubation of step (c) is performed with about 10^8 to 10^{10} mononucleated peripheral cells.

23. (twice amended) Method for preventing the reoccurrence of a tumor caused by the tumor cells against which the intact heterologous bispecific antibodies of claim 1 are directed, said method comprising administering to an individual in whom such tumor cells have appeared a tumor cell preparation prepared according to the method of claim 1.

27. (amended) Method according to claim 1 in which said rat/mouse bispecific antibody has an isotype combination selected from the group consisting of:

rat-IgG2b/mouse-IgG2a,
rat-IgG2b/mouse-IgG2b, and
rat-IgG2b/mouse-IgG3.

REMARKS

All of the changes proposed by this amendment are matters of form only. No new matter is presented, and since the amendments to the claims do no more than make explicit what was implicit in the claims as originally worded, the claim amendments are not narrowing amendments and do not give rise to amendment-based estoppel. Entry of the entire amendment and reconsideration of the application are respectfully requested.

Claim Rejections – 35 USC 112, Second Paragraph

The rewording of the claims by the above amendment addresses many of the issues raised in the rejections of claim 1-3, 13-21, and 23-30 under 35 U.S.C. 112, second paragraph, and the remaining issues are addressed by Applicants' explanations below.